```
=> d his

     (FILE 'HOME' ENTERED AT 16:23:06 ON 19 DEC 2005)

     FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 16:23:34 ON 19 DEC 2005
                E MARKS DANIEL L /AU
L1           86 S E3
                E CONE ROGER D /AU
L2          324 S E3
L3          381 S L1 OR L2
L4          272 DUP REM L3 (109 DUPLICATES REMOVED)
L5           18 S L4 AND CACHEXIA
L6            0 S L5 AND ANTAGNIST
L7            6 S L5 AND ANTAGONIST
L8            1 S CACHEXIA AND MCR4
L9        10615 S CACHEXIA
L10        6318 S MELANOCORTIN
L11         108 S L9 (L) L10
L12           0 S L11 AND ANTOGONIST
L13          58 S L11 AND ANTAGONIST
L14          37 DUP REM L13 (21 DUPLICATES REMOVED)
L15          36 S L14 AND RECEPTOR
L16          34 S L15 AND MELANOCORTIN (1W) RECEPTOR
L17           4 S L16 AND PY<2003
```

L17 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI Small molecule MC4 **receptor antagonists** for the treatment of cancer cachexia
PY **2002**
AU Vos, Tricia J.; Farrer, Cheryl A.; Che, Jennifer Lee; Caracoti, Andrei; Cohen, Seth P.; Dai, Mingshi; Eddy, Priya; Ferrara, Kristen; Forsyth, Nancy E.; Horlick, Robert A.; Jaffee, Bruce D.; Lamppu, Diana; Li, Ping; Maguire, Martin P.; Minor, Charles A.; Murray, Robert S.; Nichols, Andrew J.; Tartaglia, Lou; Zhang, Cheng
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (**2002**), MEDI-339 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CZPZ
TI Small molecule MC4 **receptor antagonists** for the treatment of cancer cachexia
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (**2002**), MEDI-339 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CZPZ
AB The **melanocortin**-4 **receptor** (MC4-R) is a seven transmembrane GPCR found in the hypothalamus. This **receptor** has been shown to play an important role in body weight regulation and energy homeostasis. Agonism of the MC4-R in. . . leads to decreased food intake and lower body weight, while antagonism has the opposite effect. We are currently pursuing MC4-R **antagonists** as potential therapeutics for the treatment of wasting disorders such as **cachexia** and anorexia. Medicinal chemical efforts toward the development of small mol. MC4-R **antagonists** for the treatment of cancer **cachexia** will be discussed.

L17 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI Identification and chemical optimization of small molecule MC4 **receptor antagonists**
PY **2002**
AU Vos, Tricia J.; Che, Jennifer Lee; Farrer, Cheryl A.; Caracoti, Andrei; Cohen, Seth P.; Dai, Mingshi; Eddy, Priya; Ferrara, Kristen; Forsyth, Nancy E.; Horlick, Robert A.; Jaffee, Bruce D.; Lamppu, Diana; Li, Ping; Maguire, Martin P.; Minor, Charles A.; Murray, Robert S.; Nichols, Andrew J.; Tartaglia, Lou; Zhang, Cheng
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (**2002**), MEDI-338 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CZPZ
TI Identification and chemical optimization of small molecule MC4 **receptor antagonists**
SO Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, 2002 (**2002**), MEDI-338 Publisher: American Chemical Society, Washington, D. C.
CODEN: 69CZPZ
AB The **melanocortin**-4 **receptor** (MC4-R) is a seven transmembrane GPCR found in the hypothalamus. This **receptor** has been shown to play an important role in body weight regulation and energy homeostasis. Agonism of the MC4-R in. . . food intake and lower body weight, while antagonism has the opposite effect. We are interested in developing small mol. MC4-R **antagonists** as potential therapeutics for treating of wasting disorders such as **cachexia** and anorexia. Identification of small mol. MC4-R **antagonists** via high-throughput screening and investigation of SAR in several series will be discussed.

L17 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI GH-releasing peptide-2 increases fat mass in mice lacking NPY: indication for a crucial mediating role of hypothalamic agouti-related protein
PY **2002**
AU Tschop, Matthias; Statnick, Michael A.; Suter, Todd M.; Heiman, Mark L.
SO Endocrinology (**2002**), 143(2), 558-568
CODEN: ENDOAO; ISSN: 0013-7227

SO Endocrinology (**2002**), 143(2), 558-568
CODEN: ENDOAO; ISSN: 0013-7227
AB . . . adiposity was thought to be mediated by hypothalamic neuropeptide Y (NPY) neurons, we investigated by which mechanism a synthetic ghrelin **receptor** agonist, GHRP-2, would generate a pos. energy balance in NPY-deficient [Npy(-/-) mice] and wild-type controls. A dose-dependent increase in body. . . mass. RQ was increased in GHRP-2-treated mice, indicating preservation of fat. Hypothalamic mRNA levels of agouti-related protein (AGRP), an orexigenic **melanocortin** **receptor** **antagonist**, increased after GHRP-2 treatment. Competitive blockade of AGRP action by **melanocortin**-**receptor** agonist MT-II prevented GHRP-induced weight gain in Npy(-/-) mice. In conclusion, chronic peripheral treatment with a ghrelin **receptor** agonist induced a pos. energy balance leading to fat gain in the absence of NPY. These effects could be mediated in part by AGRP. To date, there are few therapeutics that can produce a pos. energy balance. Ghrelin **receptor** agonists offer a treatment option for syndromes like anorexia nervosa, cancer **cachexia**, or AIDS wasting.

L17 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
TI Role of the central **melanocortin** system in **cachexia**
PY **2001**
AU Marks, Daniel L.; Ling, Nicholas; Cone, Roger D.
SO Cancer Research (**2001**), 61(4), 1432-1438
CODEN: CNREA8; ISSN: 0008-5472
TI Role of the central **melanocortin** system in **cachexia**
SO Cancer Research (**2001**), 61(4), 1432-1438
CODEN: CNREA8; ISSN: 0008-5472
AB . . . acute or chronic diseases often show disorders of nutrient balance. In some cases, a devastating state of malnutrition known as **cachexia** arises, brought about by a synergistic combination of a dramatic decrease in appetite and an increase in metabolism of fat and lean body mass. Stimulation of the hypothalamic **melanocortin** 4 **receptor** (MC4-R) produces relative anorexia and increased metabolic rate, even in a relatively starved state. Here we demonstrate that **cachexia** induced by lipopolysaccharide administration and by tumor growth is ameliorated by central MC4-R blockade. MC4-R knock-out mice or mice administered the MC3-R/MC4-R **antagonist**, agouti-related peptide, resist tumor-induced loss of lean body mass, and maintain normal circadian activity patterns during tumor growth. The final. . . is not affected in these animals, providing further support for the potential role of MC4-R antagonism in the treatment of **cachexia** in disease states.
ST **melanocortin** system **cachexia** cancer infection
IT Carcinoma
(adenocarcinoma; central **melanocortin** system in **cachexia**)
IT Anorexia
Appetite
Body weight
Cachexia
Infection
Neoplasm
Sarcoma
(central **melanocortin** system in **cachexia**)
IT Rhythm, biological
(circadian; central **melanocortin** system in **cachexia**)
IT Pituitary hormone **receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**melanocortin** 4; central **melanocortin** system in **cachexia**)
IT 128908-32-7, **Melanocortin**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(central **melanocortin** system in **cachexia**)

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	144	marks adj daniel	US-PGPUB; USPAT; DERWENT	OR	ON	2005/12/19 15:35
L2	24	cone adj roger	US-PGPUB; USPAT; DERWENT	OR	ON	2005/12/19 15:35
L3	20	l2 and melanocortin	US-PGPUB; USPAT; DERWENT	OR	ON	2005/12/19 15:36
L4	1	l1 and melanocortin	US-PGPUB; USPAT; DERWENT	OR	ON	2005/12/19 15:35
L5	6	l3 and cachexia	US-PGPUB; USPAT; DERWENT	OR	ON	2005/12/19 15:36

```
=> d his

     (FILE 'HOME' ENTERED AT 16:23:06 ON 19 DEC 2005)

     FILE 'CAPLUS, MEDLINE, BIOSIS' ENTERED AT 16:23:34 ON 19 DEC 2005
                E MARKS DANIEL L /AU
L1           86 S E3
                E CONE ROGER D /AU
L2          324 S E3
L3          381 S L1 OR L2
L4          272 DUP REM L3 (109 DUPLICATES REMOVED)
L5           18 S L4 AND CACHEXIA
L6            0 S L5 AND ANTAGNIST
L7            6 S L5 AND ANTAGONIST
```

L7 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:1032287 CAPLUS
DN 143:359317
TI The use of Melanocortin **antagonists** in **cachexia** of chronic disease
AU Scarlett, Jarrad M.; **Marks, Daniel L.**
CS Neuroscience Graduate Program, Oregon Health & Sciences University, Portland, OR, 97239, USA
SO Expert Opinion on Investigational Drugs (2005), 14(10), 1233-1240
CODEN: EOIDER; ISSN: 1354-3784
PB Ashley Publications Ltd.
DT Journal; General Review
LA English
RE.CNT 56 THERE ARE 56 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:473202 CAPLUS
DN 143:90938
TI The regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-molecule melanocortin-4 receptor **antagonist**
AU Markison, Stacy; Foster, Alan C.; Chen, Chen; Brookhart, Gregor B.; Hesse, Amy; Hoare, Sam R. J.; Fleck, Beth A.; Brown, Brock T.; **Marks, Daniel L.**
CS Neurocrine Biosciences, San Diego, CA, 92130, USA
SO Endocrinology (2005), 146(6), 2766-2773
CODEN: ENDOAO; ISSN: 0013-7227
PB Endocrine Society
DT Journal
LA English
RE.CNT 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:397861 CAPLUS
DN 143:211
TI MC4 receptor **antagonists**: a potential treatment for **cachexia**
AU Foster, Alan C.; Chen, Chen; Markison, Stacy; **Marks, Daniel L.**
CS Neurocrine Biosciences Inc, San Diego, CA, 92130, USA
SO IDrugs (2005), 8(4), 314-319
CODEN: IDRUFN; ISSN: 1369-7056
PB Thomson Scientific
DT Journal; General Review
LA English
RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2005:358774 CAPLUS
DN 142:404370
TI Anatomy and regulation of the central melanocortin system
AU **Cone, Roger D.**
CS Vollum Institute and the Center for the Study of Weight Regulation, Oregon Health and Science University, Portland, OR, 97239, USA
SO Nature Neuroscience (2005), 8(5), 571-578
CODEN: NANEFN; ISSN: 1097-6256
PB Nature Publishing Group
DT Journal; General Review
LA English
RE.CNT 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2003:472968 CAPLUS
DN 139:47578
TI Methods and reagents for using mammalian melanocortin receptor

antagonists to treat **cachexia**
IN **Marks, Daniel L.; Cone, Roger D.**
PA Oregon Health and Sciences University, USA
SO U.S. Pat. Appl. Publ., 37 pp.
CODEN: USXXCO
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2003113263	A1	20030619	US 2002-74754	20020213
PRAI US 2001-268357P	P	20010213		

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2001:183657 CAPLUS
DN 134:351464
TI Role of the central melanocortin system in **cachexia**
AU **Marks, Daniel L.**; Ling, Nicholas; **Cone, Roger D.**
CS Department of Pediatric Endocrinology, Oregon Health Sciences University, Portland, OR, 97201, USA
SO Cancer Research (2001), 61(4), 1432-1438
CODEN: CNREA8; ISSN: 0008-5472
PB American Association for Cancer Research
DT Journal
LA English
RE.CNT 60 THERE ARE 60 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L7 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
TI The use of Melanocortin **antagonists** in **cachexia** of chronic disease
AU Scarlett, Jarrad M.; **Marks, Daniel L.**
AB A review. **Cachexia** is a wasting syndrome that frequently develops in the setting of chronic diseases including cancer, congestive heart failure, chronic obstructive. . . body mass in cachectic patients. Evidence from animal models suggests a compelling link between inflammation, the central Melanocortin system, and **cachexia**. This review summarizes the current evidence supporting the role of the Melanocortin 4 (MC4) receptor subtype in **cachexia**, and discusses the development and use of small-mol. MC4 **antagonists**, which have proved to be effective in preventing the loss of lean body mass in animal models of **cachexia**. MC4 **antagonists** represent an attractive therapeutic approach for **cachexia** that may attenuate the loss of lean body mass in cachectic patients.
ST review Melanocortin **antagonist cachexia** chronic disease
IT **Cachexia**
Human
(Melanocortin **antagonists** use in **cachexia** of chronic disease)
IT Disease, animal
(chronic; Melanocortin **antagonists** use in **cachexia** of chronic disease)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4; Melanocortin **antagonists** use in **cachexia** of chronic disease)
IT 128908-32-7, Melanocortin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**antagonists**; Melanocortin **antagonists** use in **cachexia** of chronic disease)

L7 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
TI The regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-molecule melanocortin-4 receptor **antagonist**
AU . . . Foster, Alan C.; Chen, Chen; Brookhart, Gregor B.; Hesse, Amy; Hoare, Sam R. J.; Fleck, Beth A.; Brown, Brock T.; **Marks, Daniel L.**
AB **Cachexia** is metabolic disorder characterized by anorexia, an increased metabolic rate, and loss of lean body mass. It is a relatively. . . and is a pathol. feature of diseases such as cancer, HIV infection, and renal failure. Recent studies have demonstrated that **cachexia** brought about by a variety of illnesses can be attenuated or reversed by blocking activation of the melanocortin 4 subtype receptor (MC4-R) within the central nervous system. Although the potential use of central MC4-R **antagonists** for the treatment of **cachexia** was supported by these studies, utility was limited by the need to deliver these agents intracerebroventricularly. In the current study, the authors present a series of expts. demonstrating that peripheral administration of a small mol. MC4-R **antagonist** can effectively stimulate daytime (satiated) food intake as well as decrease basal metabolic rate in normal animals. Furthermore, this compound attenuated **cachexia** and preserved lean body mass in a murine cancer model. These data clearly demonstrate the potential of small mol. MC4-R **antagonists** in the treatment of **cachexia** and underscore the importance of melanocortin signaling in the development of this metabolic disorder.
ST NBI12i cancer **cachexia** melanocortin 4 receptor **antagonist**
IT **Cachexia**
(cancerous; regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)
IT Pituitary hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 1; regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 3; regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4; regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 5; regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

IT Feeding
Human
Neoplasm
(regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

IT 39332-65-5 857074-56-7, NBI 12i
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(regulation of feeding and metabolic rate and the prevention of murine cancer **cachexia** with a small-mol. melanocortin-4 receptor **antagonist**)

L7 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

TI MC4 receptor **antagonists**: a potential treatment for **cachexia**

AU Foster, Alan C.; Chen, Chen; Markison, Stacy; **Marks, Daniel L.**

AB A review. **Cachexia** (involuntary weight loss) is a devastating syndrome associated with many chronic diseases including cancer, and heart, lung, kidney and liver. . . . in these chronic diseases. Recent findings strongly indicate that blockade of central melanocortin signaling through the MC4 receptor subtype attenuates **cachexia**. This review summarizes the evidence supporting the role of MC4 receptors in **cachexia**, and highlights the progress achieved in the development of small-mol. MC4 **antagonists**, which have recently proved to be effective in animal models of **cachexia**. MC4 **antagonists** are an attractive therapeutic approach for **cachexia** that may ameliorate the loss of lean body mass in cachectic patients.

ST review MC4 receptor **antagonist cachexia**

IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4; small mol. MC4 **antagonists** are attractive therapeutic approach for **cachexia** that may ameliorate loss of lean body mass in cachectic patient)

IT **Cachexia**
Human
(small mol. MC4 **antagonists** are attractive therapeutic approach for **cachexia** that may ameliorate loss of lean body mass in cachectic patient)

L7 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

AU **Cone, Roger D.**

AB . . . is also unique from a regulatory point of view in that it is composed of fibers expressing both agonists and **antagonists** of melanocortin receptors. Given that the central melanocortin system is an active target for development of drugs for the treatment of obesity, diabetes and **cachexia**, it is important to understand the system in its full complexity, including the likelihood that the system also regulates the. . .

L7 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
TI Methods and reagents for using mammalian melanocortin receptor **antagonists** to treat **cachexia**
IN **Marks, Daniel L.; Cone, Roger D.**
AB . . . invention particularly provides such genetically engineered cells expressing the human MC-4R melanocortin receptor for screening compds. for receptor agonist and **antagonist** activity. The invention also provides screening methods using genetically engineered cells expressing the human MC-4 melanocortin receptor to specifically detect and identify agonists and **antagonists** for this melanocortin receptor. Such screening methods are provided identifying compds. with MC-4 melanocortin receptor **antagonist** activity having the capacity to influence or modify metabolism and feeding behavior, particularly pathol. feeding behavior such as illness-induced **cachexia**.
ST melanocortin receptor **antagonist** screening **cachexia** treatment
IT Energy metabolism, animal
Feeding
(**cachexia**-related; methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT Behavior
(locomotor, **cachexia**-related; methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor 4; methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT Pituitary hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(melanocortin receptor; methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT **Cachexia**
Drug screening
Genetic vectors
Human
(methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT 60-92-4, CAMP 9031-11-2, β-Galactosidase
RL: ANT (Analyte); BUU (Biological use, unclassified); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(-MC stimulated; methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT 4037-01-8, ACTH 4-10 11137-42-1, ACTH 1-39 37213-49-3, α-MSH 53697-27-1, Desacetyl-α-MSH 75921-69-6 96231-54-8, γ2-MSH 128908-32-7D, Melanocortin, analogs 168482-23-3, SHU9119 410093-94-6, Agouti-related peptide
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and reagents for screening agents modulating melanocortin receptors (MC) in relation to **cachexia** treatment)
IT 544717-03-5
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(methods and reagents for screening and using **antagonists** of melanocortin receptors (MC) to treat **cachexia**)
IT 544722-41-0 544722-42-1 544722-43-2 544722-45-4 544722-46-5 544722-47-6 544722-48-7 544722-49-8
RL: PRP (Properties)
(unclaimed nucleotide sequence; methods and reagents for using mammalian melanocortin receptor **antagonists** to treat **cachexia**)
IT 544722-44-3
RL: PRP (Properties)
(unclaimed protein sequence; methods and reagents for using mammalian

melanocortin receptor **antagonists** to treat **cachexia**
)

L7 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
TI Role of the central melanocortin system in **cachexia**
AU **Marks, Daniel L.**; Ling, Nicholas; **Cone, Roger D.**
AB . . . acute or chronic diseases often show disorders of nutrient balance. In some cases, a devastating state of malnutrition known as **cachexia** arises, brought about by a synergistic combination of a dramatic decrease in appetite and an increase in metabolism of fat. . . 4 receptor (MC4-R) produces relative anorexia and increased metabolic rate, even in a relatively starved state. Here we demonstrate that **cachexia** induced by lipopolysaccharide administration and by tumor growth is ameliorated by central MC4-R blockade. MC4-R knock-out mice or mice administered the MC3-R/MC4-R **antagonist**, agouti-related peptide, resist tumor-induced loss of lean body mass, and maintain normal circadian activity patterns during tumor growth. The final. . . is not affected in these animals, providing further support for the potential role of MC4-R antagonism in the treatment of **cachexia** in disease states.
ST melanocortin system **cachexia** cancer infection
IT Carcinoma
(adenocarcinoma; central melanocortin system in **cachexia**)
IT Anorexia
Appetite
Body weight
Cachexia
Infection
Neoplasm
Sarcoma
(central melanocortin system in **cachexia**)
IT Rhythm, biological
(circadian; central melanocortin system in **cachexia**)
IT Pituitary hormone receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(melanocortin 4; central melanocortin system in **cachexia**)
IT 128908-32-7, Melanocortin
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(central melanocortin system in **cachexia**)